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Retinal hemangioblastoma vascular detail elucidated on swept source optical coherence tomography angiography

Eugenia P. Custo Greig [a,b], Jay S. Duker [a,*]

[a] New England Eye Center, Tufts Medical Center, Boston, MA, USA
[b] Yale School of Medicine, New Haven, CT, USA

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ABSTRACT

Purpose: To report the distinct vascular pattern of a treatment-naïve retinal hemangioblastoma imaged on swept source optical coherence tomography angiography (SS-OCTA).

Observations: A 33-year-old female with a history of Von Hippel-Lindau disease presented for follow-up of bilateral retinal hemangioblastomas. Ultra-widefield fundus photography of the left eye revealed a small, juxtapapillary lesion. SS-OCTA imaging centered at the lesion identified two distinct vascular foci. Centrally, the lesion was composed of a dense capillary meshwork. Peripherally, a pattern of branching vessels with terminal budding was identified. The patient was diagnosed with a new juxtapapillary retinal hemangioblastoma.

Conclusions and Importance: SS-OCTA can visualize the in-vivo vascular structure of retinal hemangioblastomas. Early lesion identification can help in prompt diagnosis and monitoring. Further investigation is needed to assert if the branching and budding pattern described in this case report is broadly characteristic of this tumor entity.

1. Introduction

Von Hippel-Lindau (VHL) is an autosomal dominant, multi-system hereditary disorder. Ophthalmic manifestations of VHL include retinal hemangioblastomas, previously known as retinal capillary hemangiomas.[1] Studies suggest that retinal hemangioblastomas are the first manifestation of VHL in up to 77% of patients.[2] However, sporadic solitary retinal hemangioblastomas can also occur outside the setting of VHL. When associated with VHL, retinal hemangioblastomas can be the first sign of consequent disease complications such as central nervous system hemangioblastoma, renal cell carcinoma, and pancreatic neuroendocrine tumors. An ophthalmologist's ability to properly identify these lesions can start a patient on adequate disease surveillance.

Retinal hemangioblastomas most commonly arise in the retinal periphery, but can also be found on, or surrounding, the optic nerve head (ONH). ONH hemangioblastomas usually lack the characteristic tortuous feeding and draining vessels and the classic endophytic pattern associated with peripheral retinal hemangioblastomas. Thus, peripapillary retinal hemangioblastomas are often misdiagnosed as other entities including optic disc edema, peripapillary choroidal neovascularization or choroidal hemangioma.[3] Three types of retinal hemangioblastomas are recognized. The first type is an endophytic tumor that appears pink or red and lies in the inner retina, "protruding from the anterior surface of the optic disc." The second two types, sessile and exophytic, are more difficult to discern and lie within the middle and outer retina. Vascular imaging with fluorescein angiography (FA) has been used to differentiate between sessile and exophytic retinal hemangioblastomas.[3]

Optical coherence tomography angiography (OCTA) facilitates the visualization of in vivo vasculature, projected onto retinal tissue architecture. Studies comparing the use of OCTA to FA for vascular assessment of retinal hemangioblastomas show both imaging modalities are equivalent for feeder vessel identification and intrinsic blood flow visualization.[4] FA displays a greater percentage of the posterior pole and can identify lesions in the retinal periphery that might be missed on OCTA. However, OCTA confers several advantages when compared to FA, including depth-resolved flow information and fast, non-invasive serial imaging for assessment of tumor treatment response.[5] Newer swept source OCTA (SS-OCTA) devices with increased laser wavelength (~1050 nm) and scan speeds offer larger scan sizes and improved visualization of the outer retinal vasculature. Recent studies have highlighted the utility of SS-OCTA in the diagnosis of retinal hemangioblastomas located in the posterior pole.[4]

We report the case of a 33-year-old woman with a history of VHL and

* Corresponding author. Department of Ophthalmology, Tufts Medical Center, 800 Washington Street, Box 450, Boston, MA, 02111, USA.
E-mail address: jduker@tuftsmedicalcenter.org (J.S. Duker).

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multiple retinal hemangioblastomas, presenting with a small juxtapapillary lesion. Imaging with SS-OCTA and OCT revealed an intraretinal lesion, containing a branching and budding vascular network that may be characteristic of this tumor entity.

2. Case report

A 33-year-old female with a history of VHL presented for follow-up of bilateral retinal hemangioblastomas. Two years prior, a new juxtapapillary lesion was noted inferotemporally (OS) on regular ophthalmic follow up. The patient did not report any visual changes in her left eye at the time. Visual acuity in the left eye was 20/20-1, visual acuity in right eye was 20/400, consistent with prior visits.

On color fundus photography (CFP) the peripapillary lesion was identified as a hypopigmented spot inferotemporal to the optic disc, measuring approximately one quarter disc diameter (Fig. 1A). En face OCT centered at the optic disc showed a hyporeflective area inferotemporal to the ONH. The hyporeflective area seen on OCT was larger than the hypopigmented spot identified on CFP (Fig. 1B). On OCT cross-section, the lesion measured approximately 2.2 mm in greatest diameter (Fig. 1C). Cross sectional OCT showed disruption of the retinal layers between the retinal nerve fiber layer and ellipsoid zone. There were no discernible breaks or disruptions of the retinal pigment epithelium (RPE) below the tumor. Small pockets of intraretinal fluid were identified proximal to the lesion (Fig. 1C).

A 3 × 3mm scan centered at the lesion was obtained on SS-OCTA (PLEX Elite 9000; Carl Zeiss Meditec, Inc, Dublin, CA). Images were manually segmented between the inner plexiform layer and the retinal pigment epithelium to fully capture the lesion. En face projection of the manually selected slab identified two distinct vascular foci within the lesion. The first focus corresponds to the hypopigmented spot described on fundus photography and is composed of a dense vascular meshwork (Fig. 2A and B). The second focus is located superotemporal to the first, and corresponds to the hyporeflective region identified on en face OCT. This vascular focus is defined by a branching vascular pattern with terminal budding (Fig. 2A and B). An anastomosis between a branching vessel and an artery emerging from the ONH was identified within this second vascular focus (Fig. 2A and B).

Given the patient's history of VHL and the peripapillary location of the lesion, the patient was diagnosed with a new juxtapapillary retinal hemangioblastoma. Due to lack of symptoms or significant exudate, no treatment was warranted at the time of presentation. The patient is being closely followed for new vision changes or increased retinal fluid on OCT.

3. Discussion

This case report shows the utility of OCT and OCTA as diagnostic tools for the identification of retinal hemangioblastoma. OCT imaging captured the full extent of the lesion, revealing that the tumor was larger in size than fundus photography suggested. An OCT B-scan through the lesion identified that the RPE underlying the tumor remained intact. The lesion's low profile and intraretinal location are most consistent with a sessile-type lesion. Sessile lesions are difficult to identify, as they are less apparent on fundoscopy and often lack the red hue associated with endophytic lesions.[3] OCT imaging revealed the tumor's full extent and aided in its classification.

Prior studies utilizing OCTA to visualize treatment naive retinal hemangioblastoma have reported increased vascularity over the tumor surface. Lang et al. reported the case of a cystic retinal hemangioblastoma with internal flow seen on OCTA B-scan, but the lesion lacked any clear vascular pattern on en face imaging.[5] We report a juxtapapillary retinal hemangioblastoma with an internal vascular pattern identified on OCTA (Fig. 2). The tumor contained two distinct vascular foci. Centrally, the lesion is robustly vascular, composed of a dense capillary meshwork. Superotemporally, towards the lesion's periphery,

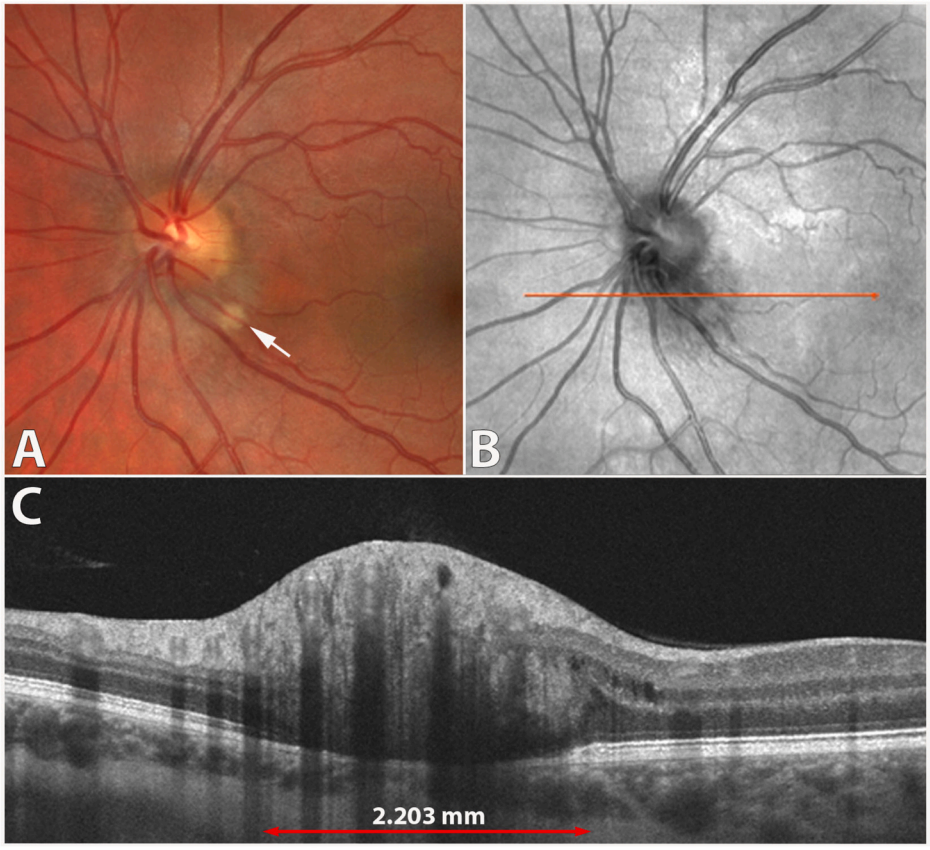

Fig. 1. Juxtapapillary retinal hemangioblastoma (OS). (A) Fundus photograph, white arrow points to juxtapapillary retinal hemangioblastoma. Lesion appears as a hypopigmented spot without clear feeding or draining vessels. (B) SD-OCT structural en face image centered at optic nerve head. Red line shows B-scan location. Hyporeflective area inferotemporal to the optic nerve head corresponds to lesion location and is larger than the hypopigmented spot seen on fundus photography. (C) B-scan through lesion shows full intraretinal extent of the lesion. Lesion measures approximately 2.2 mm in greatest diameter. RPE below the lesion is undisturbed without any notable breaks or disruptions, consistent with a sessile type retinal hemangioblastoma. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

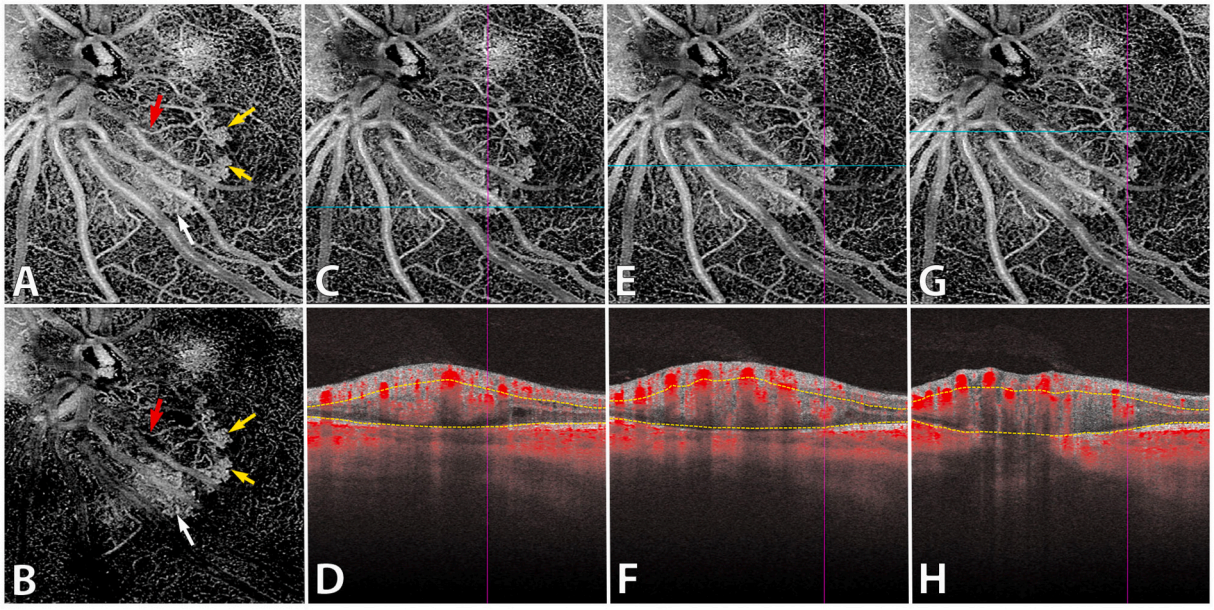

Fig. 2. SS-OCTA image of a juxtapapillary retinal hemangioblastoma. The manually segmented slab is bound by the inner plexiform layer superiorly and the retinal pigment epithelium inferiorly. (A) En face projection of the manually segmented slab without projection artifact removal. (B) En face projection of the manually segmented slab with projection artifact removal. Vascular foci are evident even after software removal of overlying retinal vasculature. (A–B) White arrow points to dense vascular focus. Yellow arrows point to branching vessels with terminal budding. Red arrow points to feeder vessel arising from a larger artery exiting the optic nerve head. (C–H) En face OCTA images with corresponding B-scans show that highlighted vascular areas correspond to internal tumor flow and not to projection artifact from overlying vasculature. (C–D) Dense vascular meshwork within the tumor has no discernible vessels and resembles the budding vascular areas highlighted by the yellow arrows. (E–H) Branching vessels with terminal budding, could represent sites of new vascular growth for the tumor. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

there is a second vascular focus composed of branching vessels with terminal budding (Fig. 2A and B). B-scans through each of these vascular foci correspond to flow pixels within the lesion, confirming that the aberrant vasculature seen on en face imaging is part of the lesion's internal vascular structure (Fig. 2C–H). The budding vessels identified on OCTA lie towards the lesion's periphery and could be sites of potential vascular growth for the tumor. Longitudinal imaging is needed to confirm this hypothesis and to determine if these new vascular buds transform into dense vascular areas at risk of exudation and related sequalae.

Retinal hemangioblastomas are intrinsically vascular lesions. Studies have found that these tumors release multiple angiogenic factors including vascular endothelial growth factor, erythropoietin and platelet-derived growth factor.[6] Interestingly, the branching and budding vascular pattern described in this report is consistent with the vascular pathology of retinal hemangioblastomas, which has been described as capillary-like, fenestrated channels surrounded by vacuolated foamy cells.[7] Though OCTA does not possess the resolution to identify cellular structures, the intertwining network of capillaries and vacuolated stromal cells reported in molecular pathology studies resembles the capillary buds we observed on imaging.

4. Conclusions

The vascular nature of retinal hemangioblastomas has been previously reported, however, little is known of the in-vivo vessel architecture of these lesions. This case highlights the utility of OCT to identify and classify these tumors, and the value of OCTA in revealing their internal vascular complexity. Further studies are needed to determine if the branching and budding pattern reported is seen in other retinal capillary hemangioblastomas. Longitudinal assessment of these tumors with OCTA could provide insight into the vascular maturation of retinal hemangioblastomas and identify biomarkers that could predict exudation.

Patient consent

Consent for publication was received from the individual whose data is presented in this case report.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Other contributions

None.

Declaration of competing interest

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References

1. Wong WT, Chew EY. Ocular von Hippel-Lindau disease: clinical update and emerging treatments. *Curr Opin Ophthalmol*. 2008;19:213–217.
2. Kreusel KM, Bechrakis NE, Krause L, Neumann HP, Foerster MH. Retinal angiomatosis in von Hippel-Lindau disease: a longitudinal ophthalmologic study. *Ophthalmology*. 2006;113:1418–1424.
3. Gass JD, Braunstein R. Sessile and exophytic capillary angiomas of the juxtapapillary retina and optic nerve head. *Arch Ophthalmol*. 1980;98:1790–1797.
4. Sagar P, Rajesh R, Shanmugam M, Konana VK, Mishra D. Comparison of optical coherence tomography angiography and fundus fluorescein angiography features of retinal capillary hemangioblastoma. *Indian J Ophthalmol*. 2018;66:872–876.
5. Lang SJ, Cakir B, Evers C, Ludwig F, Lange CA, Agostini HT. Value of optical coherence tomography angiography imaging in diagnosis and treatment of hemangioblastomas in von Hippel-lindau disease. *Ophthalmic Surg Lasers Imaging Retina*. 2016;47:935–946.
6. Chan CC, Vortmeyer AO, Chew EY, et al. VHL gene deletion and enhanced VEGF gene expression detected in the stromal cells of retinal angioma. *Arch Ophthalmol*. 1999; 117:625–630.
7. Chan CC, Collins AB, Chew EY. Molecular pathology of eyes with von Hippel-Lindau (VHL) Disease: a review. *Retina*. 2007;27:1–7.